MAY 0 4 2000

I Preby certify that this correspondence is being deposited with 1 and 2000 U.S. Postal Spring with sufficient postage as First Class Mail, in an envelope addressed to 2000 Post Issue, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 2313-1450, on the date shown below.

Dated: May 2, 2005

Signature: August 2006

09/869.414 (OSC)FW

Docket No.: 29915/6280MUS

(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Letters Patent of: Mark E. Gurney et al.

Patent No.: 6,790,610

Issued: September 14, 2004

For: ALZHEIMER'S DISEASE, SECRETASE, APP

SUBSTRATES THEREFOR, AND USES

THEREFOR

Certificate MAY 1 1 2005

of Correction

REQUEST FOR CERTIFICATE OF CORRECTION PURSUANT TO 37 CFR 1.323

MS Post Issue Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Dear Sir:

Patentees respectfully request a Certificate of Correction to be issued for the above-identified U.S. Patent correcting the patent as noted in the attached "Certificate of Correction" form PTO/SB/144. Duplicate copies of the form are attached hereto.

At column 9, lines 63-64 please delete "according to claim 14 or a vector according to claim 15 or 16" and insert -- of the invention or a vector of the invention-immediately following "polynucleotide". This correction is intended to omit references to particular claims and to add general language to make these statements clear and concise. This correction was approved by the Certificate of Correction Branch of the United States Patent and Trademark Office in parent application serial no. 09/416,901, now U.S. Patent No. 6,699,671. This correction does not add new matter to the patent.

05/05/2005 AKELECH2 00000036 6790610

01 FC:1811

100.00 OP

Patent No.: 6,790,610 Docket No.: 29915/6280MUS

Errors in the patent can be verified by reference to the application as follows:

Appln. Page #	Appln. Line #	Column # Cover page Section (54)	<u>Line #</u> 1	Error By PTO
Terminal disclaimer 3/21/04	·	Cover page Section (*)		РТО
PTO/Form/892		Cover page 2 Column 1	5 .	PTO
1	1	1	1	PTO
2	20	2	3	PTO
5	14	3	56	Applicant
6	9	4	24	Applicant
7	16 .	5	10	Applicant
8	14	5	49	Applicant
			20	
9	17	6	28	Applicant
12	12	8	6	PTO
Amendment Dated 05/27/03	Page 2	8	16	Applicant
13	4	8	37	Applicant
13	24	8	64	Applicant
13	28	9	3	Applicant
14	22	9	38	Applicant
14	24	9	40	Applicant
15	1	9	51	Applicant
15	21	10	12	Applicant
17	24	11	37	Applicant

Patent No.: 6,790,610

Appln. Page #	Appln. Line # 5	Column #	<u>Line #</u> 53	Error By Applicant
24	23	16	11	Applicant
25	19	16	48	PTO
26	2	16	65	PTO
26	29	17	37	PTO
28	17	18	38	Applicant
Amendment Dated 5/27/03	page 3, line 9	21	12,	PTO
39	9	25	12	Applicant
47	21	30	28	PTO
49	5	31	20	Applicant
51	8	32	42	Applicant
52	2	33	8	Applicant
53	10	33	60	PTO
53	12	33	63	Applicant
53	15	33	66	PTO
56	18	35	59	PTO
59	17	36	63	Applicant
64	8	39	17	PTO
64	9	39	18	PTO
64	13	39	24	PTO
64	13	39	26	PTO
64	14	39	26	PTO
66	24	40	51	Applicant

Docket No.: 29915/6280MUS

Patent No.: 6,790,610

Appln. Page # 67	Appln. Line # 5	<u>Column #</u> 40	<u>Line #</u> 67	Error By PTO
67	6	40	67	PTO
67	10	41	5	PTO
67	19	41	17	Applicant
73	23	44	50	PTO
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79	9	48	1	PTO
76	16	48	11	PTO
81	6	49	16	PTO
Amendment Dated 1/5/04	Sequence Listing pages 1-63	Sequence listing Columns 49-164		PTO
Examiner's Amendment Claim 155, lines 3-4		163 claim 1	43-44	PTO
Examiner's Amendment Claim 155, lines 8-10		163 claim 1	51-54	PTO
Examiner's Amendment Claim 162, line 1		164 claim 6	45	PTO
Examiner's Amendment Claim 164, line 1		164 claim 8	50	PTO
Examiner's Amendment Claim 166, line 1		164 claim 10	56	PTO

At least one of the errors were found in the application as filed by applicant. Our check in the amount of \$100.00 covering the fee set forth in 37 CFR 1.20(a) is enclosed.

Patent No.: 6,790,610 Docket No.: 29915/6280MUS

The errors now sought to be corrected are inadvertent typographical errors the correction of which does not involve new matter or require reexamination.

Transmitted herewith is a proposed Certificate of Correction effecting such amendment. Patentee respectfully solicits the granting of the requested Certificate of Correction.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 13-2855, under Order No. 29915/6280MUS. A duplicate copy of this paper is enclosed.

Dated: May 2, 2005

Respectfully submitted,

Jeanne M. Brashear

Registration No.: 56,301

MARSHALL, GERSTEIN & BORUN LLP

233 S. Wacker Drive, Suite 6300

Sears Tower

Chicago, Illinois 60606-6357

(312) 474-6300

Agent for Applicant

Approved for use through 04/30/2007. OMB 0651-0033

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

PATENT NO.

6,790,610

DATED

September 14, 2004

INVENTOR(S)

Mark E. Gurney et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In the Cover Sheet:

At Section 54, column 1, please delete "Disease, Secretase" and insert -- Disease Secretase--

At Section (*), column 1, please insert -- This patent is subject to a terminal disclaimer ---.

On page 2, column 1, line 5, please delete "th" and insert --the--.

In the Specification:

At Column 1, line 1, please delete "Disease, Secretase" and insert -- Disease Secretase--.

At Column 2, line 3, please delete "a-site" and insert --α site--.

At Column 3, line 56, please insert -- of-- before "those".

At Column 4, line 24, please delete "lease" and insert -- least --.

At Column 5, line 10, please insert --to-- before "any".

At Column 5, line 49, please insert --of-- before "those".

At Column 6, line 28, please delete "lease" and insert -- least--.

At Column 8, line 6, please insert --iii) select the cells which produce the critical peptide.-after "APP."

At Column 8, line 16, please insert --(SEQ ID NO: 74)-- after "P2".

At Column 8, line 37, please delete "has" and insert --as--.

At Column 8, line 64, please delete "Measurment" and insert -- Measurement--

At Column 9, line 3, please delete "reporter-protein" and insert --reporter protein--.

At Column 9, line 38, please delete "construct" and insert --constructed--.

At Column 9, line 40, please delete "streches" and insert --stretches--.

At Column 9, line 51, please delete "recombinant" and insert --recombinant--.

At Column 10, line 12, please delete "hyrdrophobic" and insert --hydrophobic--.

MAILING ADDRESS OF SENDER:

Jeanne M. Brashear MARSHALL, GERSTEIN & BORUN LLP 233 S. Wacker Drive, Suite 6300 Sears Tower Chicago, Illinois 60606-6357

PATENT NO. 6,790,610

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In the Specification, (cont'd):

At Column 11, line 37, please delete "oassays" and insert --bioassays--.

At Column 11, line 53, please delete "on" and insert -- one --.

At Column 16, line 11, please delete "Fig. 11" and insert -- Fig. 12--.

At Column 16, line 48, please delete "I)" and insert --ID--.

At Column 16, line 65, please delete "Glutarnine" and insert -- Glutamine--.

At Column 17, line 37, please delete "α-secretase" and insert -- β-secretase--.

At Column 18, line 38, please delete "possible" and insert --possibly--.

At Column 21, line 12, please delete "6" and insert --6,--

At Column 25, line 12, please delete "embyonic" and --embryonic--.

At column 30, line 28, please delete "Hu-ASPI" and insert -- Hu-asp1--.

At column 31, line 20, please delete "sequence" and insert --sequenced--.

At column 32, line 42, please insert --to-- before "contain".

At column 33, line 8, please delete "manufacture" and insert --manufacturer--.

At column 33, line 60, please delete "Phospho1mager" and insert -- PhosphorImager--.

At column 33, line 63, please delete "is" and insert --in--.

At column 33, line 66, please delete "CDNA" and insert --cDNA--.

At column 35, line 59, please delete "AP" and insert -- Aβ--.

At column 36, line 63, please delete "prorietary" and insert --proprietary--.

At column 39, line 17, please delete "AP" and insert -- Aβ--.

At column 39, line 18, please delete "AP" and insert --Aβ--.

At column 39, line 24, please delete "AP" and insert --Aβ--.

At column 39, line 26, please delete "P42" and insert --β42--.

At column 39, line 26, please delete "y-secretase" and insert --γ-secretase--. At column 40, line 51, please delete "Ab" and insert --Aβ--.

At column 40, line 67, please delete "βP40" and insert --Aβ40--. At column 40, line 67, please delete "βP42" and insert --Aβ42--. At column 41, line 5, please delete "βP42" and insert --Aβ42--.

At column 41, line 17, please delete "Ab." and insert --Aβ.--.

At column 44, line 50, please delete "internediate" and insert --intermediate--.

At column 45, line 37, please delete "20" and insert --20--.

MAILING ADDRESS OF SENDER:

Jeanne M. Brashear MARSHALL, GERSTEIN & BORUN LLP 233 S. Wacker Drive, Suite 6300 **Sears Tower** Chicago, Illinois 60606-6357

PATENT NO. 6,790,610

Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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6,790,610

DATED

hereto.

September 14, 2004

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Mark E. Gurney et al.

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In the Specification, (cont'd):

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At column 45, line 65, please delete "Hu-ASp2(b)" and insert --Hu-Asp2(b)--.

At column 46, line 65, please delete "prepared" and insert --prepare--.

At column 48, line 1, please delete "(1/250)" and insert --(1/2500)--.

At column 48, line 11, please delete "KI" and insert -- K1--.

At column 49, line 16, please delete "Swedigh" and insert -- Swedish--.

In the Sequence Listing:

Please delete the sequence listing as published and replace with the paper copy attached

In the Claims:

In claim 1, at column 163, lines 43-44, please delete "FIG. 3 (SEQ ID NO: 4)," and insert --FIG. 4, (SEQ ID NO: 3),--.

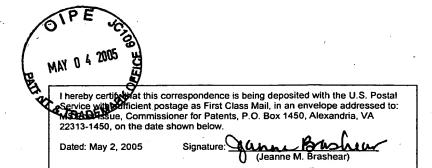
In claim 1, at column 163, lines 51-54, please delete ", and wherein the polypeptide exhibits aspartyl protease activity involved in processing APP into amyloid beta." and insert --.--.

> In claim 6, at column 164, line 45, please delete "A host" and insert -- An isolated host--. In claim 8, at column 164, line 50, please delete "derived from" and insert -- that is---In claim 10, at column 164, line 56, please delete "A host" and insert -- An isolated host--.

MAILING ADDRESS OF SENDER:

Sharon M. Sintich MARSHALL, GERSTEIN & BORUN LLP 233 S. Wacker Drive, Suite 6300 Sears Tower Chicago, Illinois 60606-6357

PATENT NO. 6,790,610



Docket No.: 29915/6280MUS

(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Patent No.: 6,790,610

Issued: September 14, 2004

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SUBSTRATES THEREFOR, AND USES

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2	20	2	3	PTO
5	14	3	56	Applicant
6	9	4	24	Applicant
7	16	5	10	Applicant
8	14	5	49	Applicant
•				
9	17	6	28	Applicant
12	12	8	6	PTO
Amendment Dated 05/27/03	Page 2	8	16	Applicant
13	4	8	37	Applicant
13	24	8	64	Applicant
13	28	9	3	Applicant
14	22	9	38	Applicant
14	24	9	40	Applicant
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17	24	11	37	Applicant
		•		

Appln. Page #	Appln. Line #	Column #	<u>Line #</u> 53	Error By Applicant
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28	17	18	38	Applicant
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39	9	25	12	Applicant
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52	2	33	8	Applicant
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64	13	39	26	PTO
64	14	39	26	PTO
66	24	40	51	Applicant

Patent No.: 6,790,610

Appln. Page # 67	Appln. Line # 5	<u>Column #</u> 40	<u>Line #</u> 67	Error By PTO
67	6	40	67	PTO -
67	10	41	5	PTO
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Examiner's Amendment Claim 155, lines 8-10		163 claim 1	51-54	PTO
Examiner's Amendment Claim 162, line 1		164 claim 6	45	PTO
Examiner's Amendment Claim 164, line 1		164 claim 8	50	PTO
Examiner's Amendment Claim 166, line 1		164 claim 10	56	PTO

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Dated: May 2, 2005

Respectfully submitted,

Jeanne M. Brashear

Registration No.: 56,301

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233 S. Wacker Drive, Suite 6300

Sears Tower

Chicago, Illinois 60606-6357

(312) 474-6300

Agent for Applicant

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6,790,610

DATED

September 14, 2004

INVENTOR(S)

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At Column 3, line 56, please insert --of-- before "those".

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At Column 5, line 10, please insert --to-- before "any".

At Column 5, line 49, please insert -- of-- before "those".

At Column 6, line 28, please delete "lease" and insert --least--.

At Column 8, line 6, please insert --iii) select the cells which produce the critical peptide.--after "APP,".

At Column 8, line 16, please insert -- (SEQ ID NO: 74)-- after "P2".

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At Column 9, line 3, please delete "reporter-protein" and insert --reporter protein--.

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At Column 9, line 51, please delete "recombinant" and insert --recombinant--.

At Column 10, line 12, please delete "hyrdrophobic" and insert --hydrophobic--.

MAILING ADDRESS OF SENDER:

Jeanne M. Brashear MARSHALL, GERSTEIN & BORUN LLP 233 S. Wacker Drive, Suite 6300 Sears Tower Chicago, Illinois 60606-6357 PATENT NO. 6,790,610

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At Column 11, line 53, please delete "on" and insert -- one --.

At Column 16, line 11, please delete "Fig. 11" and insert -- Fig. 12--.

At Column 16, line 48, please delete "I)" and insert --ID--.
At Column 16, line 65, please delete "Glutarnine" and insert --Glutarnine--.

At Column 17, line 37, please delete " α -secretase" and insert -- β -secretase--.

At Column 18, line 38, please delete "possible" and insert --possibly--.

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At column 33, line 8, please delete "manufacture" and insert --manufacturer--.

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At column 36, line 63, please delete "prorietary" and insert --proprietary--.

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At column 39, line 18, please delete "AP" and insert -- Aβ--.

At column 39, line 24, please delete "AP" and insert -- Aβ--.

At column 39, line 26, please delete "P42" and insert --β42--.

At column 39, line 26, please delete "y-secretase" and insert --y-secretase--.

At column 40, line 51, please delete "Ab" and insert --Aβ--.

At column 40, line 51, please delete "βP40" and insert --Aβ40--. At column 40, line 67, please delete "βP42" and insert --Aβ42--. At column 41, line 5, please delete "βP42" and insert --Aβ42--. At column 41, line 17, please delete "Ab." and insert --Aβ.--.

At column 44, line 50, please delete "internediate" and insert --intermediate--.

At column 45, line 37, please delete "20" and insert --20--.

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At column 48, line 11, please delete "KI" and insert -- K1--.

At column 49, line 16, please delete "Swedigh" and insert -- Swedish--.

In the Sequence Listing:

Please delete the sequence listing as published and replace with the paper copy attached

hereto.

In the Claims:

In claim 1, at column 163, lines 43-44, please delete "FIG. 3 (SEQ ID NO: 4)," and insert --FIG. 4, (SEQ ID NO: 3),--.

In claim 1, at column 163, lines 51-54, please delete ", and wherein the polypeptide exhibits aspartyl protease activity involved in processing APP into amyloid beta." and insert -----

In claim 6, at column 164, line 45, please delete "A host" and insert --An isolated host--. In claim 8, at column 164, line 50, please delete "derived from" and insert -- that is--. In claim 10, at column 164, line 56, please delete "A host" and insert --An isolated host--.

MAILING ADDRESS OF SENDER:

Sharon M. Sintich MARSHALL, GERSTEIN & BORUN LLP 233 S. Wacker Drive, Suite 6300 Sears Tower Chicago, Illinois 60606-6357 PATENT NO. 6,790,610



SEQUENCE LISTING

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Ile Val Ile Thr Leu Val Met Leu Lys Lys Gln Tyr Thr Ser Ile
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Ile Pro Tyr Arg Cys Leu Val Gly Glu Phe Val Ser Asp Ala Leu Leu 115 120 125

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Trp Trp Gly Gly Ala Asp Thr Asp Tyr Ala Asp Gly Ser Glu Asp Lys 210 215 220

Val Val Glu Val Ala Glu Glu Glu Val Ala Glu Val Glu Glu 225 230 235 240

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His His Gly Val Val Glu Val Asp Ala Ala Val Thr Pro Glu Glu Arg
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Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser 305 310 315 320

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gctgccatca ctgaatcaga caagttcttc atcaacggct ccaactggga aggcatcctg 480
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gaccactege tgtacacagg cagtetetgg tatacaceca teeggeggga gtggtattat 720
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<213> Homo sapiens
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Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg
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Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile 120 Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu 150 155 Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro 165 170 Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro Asn Leu Phe Ser 185 Leu His Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu 200 Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu 215 Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr 230 235 Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met 250 Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr 265 Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser 280 Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu 295 Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp 345 Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val

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Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys
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His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val
Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu
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Ser
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<211> 1278
<212> DNA
<213> Homo sapiens
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<211> 425
<212> PRT
<213> Homo sapiens
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Ile Ser Asp Ser Pro Leu Asp Ser Gly Ile Glu Thr Asp Gly Ser Phe
             20
                                 25
Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr
Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val
Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe
Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu
                                     90
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Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu
100 105 110

Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val 115 120 125

Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn 130 135 140

Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala 145 150 155 160

Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln
165 170 175

Thr His Val Pro Asn Leu Phe Ser Leu His Leu Cys Gly Ala Gly Phe 180 185 190

Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile 195 200 205

Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr 210 215 220

Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu 225 230 235 240

Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp 245 250 255

Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys 260 265 270

Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu 275 280 285

Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln 290 295 300

Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu 305 310 315 320

Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln 325 335

Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys 340 345 350

Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala 355 360 365

Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg 370 380

Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr 385 390 395 400

Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly 405 410 415

Tyr Asn Ile Pro Gln Thr Asp Glu Ser 420 425

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<212> DNA
<213> Homo sapiens
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gtggagatgg tggacaacct gaggggcaag tcggggcagg gctactacgt ggagatgacc 240
gtgggcagcc ccccgcagac gctcaacatc ctggtggata caggcagcag taactttgca 300
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cccctcaacc agtctgaagt gctggcctct gtcggaggga gcatgatcat tggaggtatc 720
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gaagactgtg gctacaacat tccacagaca gatgagtcat ga
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<211> 453
<212> PRT
<213> Homo sapiens
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Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser
Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp
Glu Glu Pro Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr
Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser
Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
                               105
Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val
Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp
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Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile 150 155 Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp 165 170 Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln 210 215 220 Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile 230 Asp. His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg 250 Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val 280 Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala 295 Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr . 330 Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val 345 Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala 375 Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala 410 Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu 420 425 Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu Ser

450

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<213> Homo sapiens
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gtgggcagcc ccccgcagac gctcaacatc ctggtggata caggcagcag taactttgca 300
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ctgggcaccg acctggtaag catccccat ggccccaacg tcactgtgcg tgccaacatt 480
gctgccatca ctgaatcaga caagttette atcaacgget ccaactggga aggcatcetg 540
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<211> 459
<212> PRT
<213> Homo sapiens
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Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser
Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp
Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
                        55
                                            60
Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr
Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser
Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
           100
                               105
Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val
Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp
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Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile 150 155 Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp 170 Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp 185 Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln 215 Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile 230 235 Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val 280 Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala 295 Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr 325 Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val 345 Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala 375 Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala 410 Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu 420 425 Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu Ser His His His His His 455

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 <213> Homo sapiens
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Ser Ser Leu Val Arg His Arg Trp Lys
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 <210> 34
 <211> 19
 <212> PRT
<213> Homo sapiens
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 Ser Glu Gln Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp Ile Ser
Leu Leu Lys
<210> 35
<211> 29
<212> DNA
 <213> Homo sapiens
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 <212> DNA
<213> Homo sapiens
<400> 36
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<210> 37
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<213> Homo sapiens
<400> 37
gatcgatgac tatctctgac tctccgcgtg aacaggacg
                                                                     39
<210> 38
<211> 39
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<213> Homo sapiens
<400> 38
                                                                     39
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<210> 39
<211> 77
<212> DNA
 <213> Artificial Sequence
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<223> Description of Artificial Sequence: Hu-Asp2
eggeateegg etgeecetge gtageggtet gggtggtget ceaetgggte tgegtetgee 60
ccgggagacc gacgaag
<210> 40
<211> 77
<212> DNA
<213> Artificial Sequence
<223> Description of Artificial Sequence: Hu-Asp2
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ggggcagccg gatgccg
<210> 41
<211> 51
<212> DNA
<213> Artificial Sequence
<223> Description of Artificial Sequence: Caspase 8
      Cleavage Site
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                                                                    51
<210> 42
<211> 51
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Caspase 8
      Cleavage Site
<400> 42
gatccgtcgg tttcgatacc agagtccagc ggagagtcag agatagtcat c
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<210> 43
<211> 32
<212> DNA
<213> Homo sapiens
aaggatcctt tgtggagatg gtggacaacc tg
                                                                    32
<210> 44
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<212> DNA
<213> Homo sapiens
gaaagctttc atgactcatc tgtctgtgga atgttg
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<210> 45
<211> 24
<212> DNA
<213> Artificial Sequence
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<220>
<223> Description of Artificial Sequence: 6-His tag
<400> 45
                                                                    24
gatcgcatca tcaccatcac catg
<210> 46
<211> 24
<212> DNA
<213> Artificial Sequence
<223> Description of Artificial Sequence: 6-His tag
<400> 46
gatccatggt gatggtgatg atgc
                                                                    24
<210> 47
<211> 22
<212> DNA
<213> Artificial Sequence
<223> Description of Artificial Sequence: primer
<400> 47
                                                                    22
gactgaccac tcgaccaggt tc
<210> 48
<211> 51
<212> DNA
<213> Artificial Sequence
<223> Description of Artificial Sequence: primer
                                                                    51
cgaattaaat tccagcacac tggctacttc ttgttctgca tctcaaagaa c
<210> 49
<211> 26
<212> DNA
<213> Artificial Sequence
<223> Description of Artificial Sequence: primer
<400> 49
cgaattaaat tccagcacac tggcta
                                                                    26
<210> 50
<211> 1287
<212> DNA
<213> Artificial Sequence
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<223> Description of Artificial Sequence: Hu-Asp2(b)
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ggcacccage acggcatecg getgeceetg cgcageggee tgggggggege ccccetgggg 120
ctgeggetge ccegggagae cgacgaagag ccegaggage ccggceggag gggcagettt 180
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gtggagatgg tggacaacct gaggggcaag tcggggcagg gctactacgt ggagatgacc 240
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gtgggtgetg ecceeacce ettectgeat egetactace agaggeaget gtecageaca 360
taccgggacc tccggaaggg tgtgtatgtg ccctacaccc agggcaagtg ggaaggggag 420
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<210> 51
<211> 428
<212> PRT
<213> Artificial Sequence
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<223> Description of Artificial Sequence: Hu-Asp2(b)
      delta TM
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Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser
Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp
Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr
Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser
                 85
Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
                                105
Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val
        115
Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp
                        135
                                            140
Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile
Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
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Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu 260 265 270

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Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val 290 295 300

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105

100

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375

370

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Ala Leu Glu Val Pro Thr Asp Gly Asn Ala Gly Leu Leu Ala Glu Pro

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Thr Gln Glu Pro Leu Ala Arg Asp Pro Val Lys Leu Pro Thr Thr Ala 360 Ala Ser Thr Pro Asp Ala Val Asp Lys Tyr Leu Glu Thr Pro Gly Asp 375 Glu Asn Glu His Ala His Phe Gln Lys Ala Lys Glu Arg Leu Glu Ala Lys His Arg Glu Arg Met Ser Gln Val Met Arg Glu Trp Glu Glu Ala Glu Arg Gln Ala Lys Asn Leu Pro Lys Ala Asp Lys Lys Ala Val Ile Gln His Phe Gln Glu Lys Val Glu Ser Leu Glu Gln Glu Ala Ala Asn Glu Arg Gln Gln Leu Val Glu Thr His Met Ala Arg Val Glu Ala Met Leu Asn Asp Arg Arg Leu Ala Leu Glu Asn Tyr Ile Thr Ala Leu 475 Gln Ala Val Pro Pro Arg Pro Arg His Val Phe Asn Met Leu Lys Lys 490 Tyr Val Arg Ala Glu Gln Lys Asp Arg Gln His Thr Leu Lys His Phe 500 505 Glu His Val Arg Met Val Asp Pro Lys Lys Ala Ala Gln Ile Arg Ser Gln Val Met Thr His Leu Arg Val Ile Tyr Glu Arg Met Asn Gln Ser 535 Leu Ser Leu Leu Tyr Asn Val Pro Ala Val Ala Glu Glu Ile Gln Asp 550 555 Glu Val Asp Glu Leu Leu Gln Lys Glu Gln Asn Tyr Ser Asp Asp Val Leu Ala Asn Met Ile Ser Glu Pro Arg Ile Ser Tyr Gly Asn Asp Ala Leu Met Pro Ser Leu Thr Glu Thr Lys Thr Thr Val Glu Leu Leu Pro 600 Val Asn Gly Glu Phe Ser Leu Asp Asp Leu Gln Pro Trp His Ser Phe 615 Gly Ala Asp Ser Val Pro Ala Asn Thr Glu Asn Glu Val Glu Pro Val Asp Ala Arg Pro Ala Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser 645 Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Lys Met Asp 665 Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys Leu 675 680

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Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp 50 55 60

Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu 65 70 75 80

Gln Ile Thr Asn Val Val Glu Ala Asn Gln Pro Val Thr Ile Gln Asn 85 90 95

Trp Cys Lys Arg Gly Arg Lys Gln Cys Lys Thr His Pro His Phe Val

Ile Pro Tyr Arg Cys Leu Val Gly Glu Phe Val Ser Asp Ala Leu Leu 115 120 125

Val Pro Asp Lys Cys Lys Phe Leu His Gln Glu Arg Met Asp Val Cys 130 135 140

Glu Thr His Leu His Trp His Thr Val Ala Lys Glu Thr Cys Ser Glu 145 150 155 160

Lys Ser Thr Asn Leu His Asp Tyr Gly Met Leu Leu Pro Cys Gly Ile 165 170 175

Asp Lys Phe Arg Gly Val Glu Phe Val Cys Cys Pro Leu Ala Glu Glu 180 185 190

Ser Asp Asn Val Asp Ser Ala Asp Ala Glu Glu Asp Asp Ser Asp Val 195 200 205

Trp Trp Gly Gly Ala Asp Thr Asp Tyr Ala Asp Gly Ser Glu Asp Lys 210 215 220

Val Val Glu Val Ala Glu Glu Glu Glu Val Ala Glu Val Glu Glu 225 230 235 240

Glu Ala Asp Asp Asp Glu Asp Glu Asp Gly Asp Glu Val Glu Glu 245 250 255

Glu Ala Glu Glu Pro Tyr Glu Glu Ala Thr Glu Arg Thr Thr Ser Ile
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Ala Thr Thr Thr Thr Thr Thr Glu Ser Val Glu Glu Val Val Arg

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Pro Ala Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser Gly Leu Thr 625 630 635 Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Lys Met Asp Ala Glu Phe 650 Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys Leu Val Phe Phe 665 Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Val Ile Val Ile Thr Leu Val Met Leu 695 700 Lys Lys Lys Gln Tyr Thr Ser Ile His His Gly Val Val Glu Val Asp Ala Ala Val Thr Pro Glu Glu Arg His Leu Ser Lys Met Gln Gln Asn 725 730 Gly Tyr Glu Asn Pro Thr Tyr Lys Phe Phe Glu Gln Met Gln Asn Lys 745 Lys <210> 62 <211> 8 <212> PRT <213> Artificial Sequence <223> Description of Artificial Sequence: Synthetic Peptide <400> 62 Leu Glu Val Leu Phe Gln Gly Pro 5 <210> 63 <211> 10 <212> PRT <213> Artificial Sequence <223> Description of Artificial Sequence: Synthetic Peptide Ser Glu Val Asn Leu Asp Ala Glu Phe Arg <210> 64 <211> 10 <212> PRT <213> Artificial Sequence <223> Description of Artificial Sequence: Synthetic Peptide

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